

Multimodality Imaging in Tuberous Sclerosis – A Case Study

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Abstract :

Tuberous sclerosis is a neurocutaneous syndrome that has been classically described to be associated with the triad of seizures, mental retardation and facial adenoma sebaceum. However, this triad does not occur in the complete set of patients diagnosed with the condition. Therefore, diagnosis could get delayed in these patients or the condition may not come to clinical attention until late in its course or until complications develop. Therefore early imaging plays a key role in the diagnosis of this common neurocutaneous syndrome and in the management of the same.

Keywords : Neurocutaneous syndrome, adenoma sebaceum, seizures.

Introduction :

Tuberous sclerosis is an autosomal-dominant disorder. Approximately 50% of cases are inherited and 50% are sporadic. Manifestations of tuberous sclerosis can become apparent in persons of any age, but most patients have clinical symptoms before they are aged 10 years. The classic form of the disease is the triad of seizures, mental retardation, and adenoma sebaceum, which is a papular facial nevus more accurately termed facial angiofibroma. This classic appearance occurs in less than half of patients, probably in one third.

Abnormal radiologic findings are important in diagnosing this disease and include CNS lesions of cortical hamartomas, white-matter abnormalities, and subependymal nodules (ie, hamartomas). Retinal lesions, non-atheromatous vascular stenoses and aneurysms, and mild ventricular enlargement without astrocytomas can be present.

Clinical History and Imaging Findings

A 38 year old female patient underwent evaluation in the surgery department for abdominal pain and increasing abdominal girth. Clinical evaluation revealed bilateral ballotable masses in the abdomen. Patient also showed a papular pigmentation of the malar eminences. Patient was assessed to have normal mental status. No seizure history was elicited.

CT study of the abdomen shows bilaterally grossly enlarged angiomyolipomatous kidneys with gross

architectural distortion. Renal excretion was maintained. (Fig 1,2) Multiple vertebral bony islands were seen in the thoracolumbar spine. (Fig 3,4)

Basal sections of the thorax showed a low attenuation lesion in the right middle lobe reminiscent of a cystic lymphangiomyoma.

CT and MRI studies of the brain were undertaken and showed multiple calcified subependymal nodules, some of which showed enhancement. (Fig 5,6) Multiple cortical tubers were seen as well, confirming the diagnosis of Tuberous Sclerosis. (Fig 7,8)

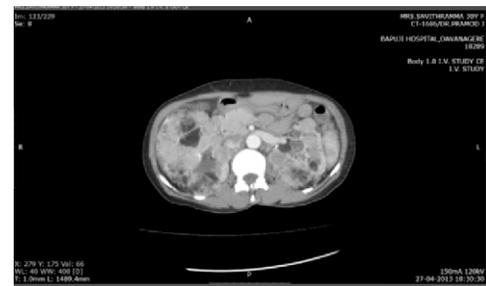


Fig 1 : Arterial phase enhanced CT scan of the abdomen demonstrated bilaterally massively enlarged, deformed kidneys with multiple angiomyolipomas



Fig 2 : Coronal reconstruction shows the enlarged kidneys with multiple renal angiomyolipomas.

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Fig 3 : Pulmonary widening shows a cystic lymphangioliomyoma in the right middle lobe.



Fig 4 : Bony window in sagittal reconstruction shows multiple bony islands in the thoracolumbar segments.



Fig 5 : CT Scan of the brain shows multiple calcified subependymal nodules.



Fig 6 : Some of the nodules show enhancement following contrast administration. One calcified nodule is seen in the left ventricle frontal horn.



Fig 7 : FLAIR axial section shows cortical tuber in the anterior left parietal region and right parietal region.



Fig 8 : FLAIR axial section shows left frontal and parietal cortical tubers.

Discussion:

Tuberous sclerosis is an autosomal-dominant disorder. Approximately 50% of cases are inherited and 50% are sporadic. The severity of the disease appears to reflect the variable penetrance. The disease is caused by mutations in either the *TSC1* gene, on chromosome 9q34, or the *TSC2* gene, on chromosome 16p13.3.¹⁻⁴

Manifestations of tuberous sclerosis can become apparent in persons of any age, but most patients have clinical symptoms before they are aged 10 years. The classic form of the disease is the triad of seizures, mental retardation, and adenoma sebaceum, This classic appearance occurs in less than half of patients, probably in one third.

Abnormal radiologic findings are important in diagnosing this disease and include CNS lesions of cortical hamartomas, white-matter abnormalities, and subependymal nodules. Patients also have subependymal giant cell astrocytomas. These intracranial neoplasms can result in obstructive hydrocephalus. Retinal lesions, nonatheromatous vascular stenoses and aneurysms, and mild ventricular enlargement without astrocytomas can be present.

Tuberous sclerosis is a multisystemic disorder. Non-CNS lesions of tuberous sclerosis include cutaneous manifestations. In addition to the lesions mentioned above, these include vitiligo and subungual patches. Findings also are observed in the heart; lungs; kidneys; skeleton; and, occasionally, liver, spleen, and pancreas. Computed tomography (CT) and magnetic resonance imaging (MRI) of the brain are the most sensitive screening imaging studies. Currently, MRI is considered the modality of choice for the evaluation of the brain in patients with diagnosed or suspected tuberous sclerosis. CT is the modality of choice for evaluating renal lesions because of its ability to delineate cystic from solid lesions and lipid-containing angiomyolipomas.^{5,6} CT is much less sensitive than MRI in the identification of cortical hamartomas and neuronal migration streaks. MRI is less sensitive than CT in the identification of calcifications of the brain.

Abnormal radiologic findings are important in diagnosing this disease and include CNS lesions of cortical hamartomas, white-matter abnormalities, and subependymal nodules (ie, hamartomas).

Most findings detectable on plain radiographs are musculoskeletal or thoracic. Changes include osteoporosis and cystic defects in the metacarpals, metatarsals, and/or phalanges. Erosions of the tufts of the distal phalanges, the result of ungual angiomyofibromas, may be observed. Heterogeneous sclerosis can affect the

entire axial skeleton. Multiple bone islands with an apparent natural propensity for the diploic space may be observed. Macroductyly and expansile-enhanced bone density that is restricted to a single rib are described. Plain skull films often reveal sclerosis or widening of the diploic space, which is related to the administration of phenytoin.

Chest radiographs rarely can depict evidence of interstitial fibrosis or honeycombing. Occasionally, the appearance of the chest is compatible with its appearance in lymphangioliomyomatosis (LAM). The connection between tuberous sclerosis and LAM is unclear. Pneumothorax is an infrequent complication in interstitial fibrosis and LAM. Approximately one fourth of patients can have cardiac rhabdomyomas, which places these patients at risk for congestive heart failure.

Renal angiomyolipomas occur in 50-90% of patients but only rarely contain enough adipose tissue to be observed on plain radiographs. Hamartomatous polyps can be present in the colon. Gastric polyposis also can occur; this can be depicted on barium studies. CT readily depicts calcified cortical tubers and calcified subependymal nodules; the frequency of their calcification increases with patient age. Angiomyolipomas often have low attenuation values if they contain sufficient fat, but they are indistinguishable from other renal tumors if they contain little or no lipid. Varying amounts of nonlipid tissue and hemorrhage can be visualized on CT scans of angiomyolipomas. Generally, calcification is not seen in angiomyolipomas.

CT reveals the cystic and interstitial changes in the lungs of patients with tuberous sclerosis. Abnormal findings include interstitial thickening, alveolar destruction, and honeycomb lung; these are pathologically indistinguishable from those in lymphangioliomyomatosis (LAM). Some authors consider LAM to be a *forme fruste* of tuberous sclerosis.

MRI is the imaging modality of choice for evaluating intracranial lesions of tuberous sclerosis. Cortical tubers, or hamartomas, are the most characteristic lesions of tuberous sclerosis; they are detected on MRIs in 95% of patients. In neonates and young children, the cortical tubers and subependymal nodules are hyperintense on T1-weighted images and hypointense on T2-weighted images. In older children and adults, the cortical and

subependymal lesions are isointense or hypointense on T1-weighted images. They are hyperintense relative to gray matter, as well as white matter, on T2-weighted images, depending on the presence of calcification.^{7,8}

Enhancement of cortical and subcortical lesions is uncommon and occurs in fewer than 5% of the cases. When enhancement is present, it does not suggest neoplasia. Enhancement of subependymal nodules is common, and it is better visualized on MRIs than on CT scans.

MRIs depict several distinct patterns of white matter lesions, White matter lesions in older children and adults typically are isointense or hypointense on T1-weighted images compared with white matter and hyperintense on T2-weighted images compared with gray matter and white matter.

Subependymal nodules are detected in 95% of patients. Subependymal giant cell astrocytomas appear inhomogeneous, with intense enhancement after the administration of contrast material. The fat in angiomyolipomas usually can be recognized.

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